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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,913	03/16/2000	STEPHEN A. UDEM	33.359-01P	3738

7590 12/05/2001

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	11

DATE MAILED: 12/05/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,913	UDEM ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *5-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election without traverse of Group I in Paper No. 10 is acknowledged.

Specification

Applicant is required to update the status (pending, allowed, ect.) of all parent priority applications in the first line of the specification.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because: It does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation. Specifically, the post-office address and address information is missing for the fourth inventor.

Sequence listing

Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 7, is attached to the instant Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are rendered indefinite in that they describe mutations by an amino acid number without providing which viral strain numbering system is used. There appears to be great genetic diversity among RSV (Venter et al. Journal of General Virology, 2001) subgroup A and B which can give rise to frame shift mutations, wherein an amino acid is either deleted or inserted which in turn has an effect on the numbering of the amino acids. Therefore, describing mutations by an arbitrary number without giving the clone from which the numbering system is derived renders the claim indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for attenuated viral mutants that have multiple mutations (see table 21 and 22), does not reasonably provide enablement for ~~of~~ achieving an attenuated RSV virus by making a single mutation in the RNA polymerase gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims recite

the generation of an attenuated RSV, and the specification provides sequence examples which are disclosed on tables 21 and 22. The mutations disclosed in table 21 and 22 were not recombinantly generated, they were sequenced from a previously isolated virus that was chemically modified and plaque purified.

Claim 2 recites specific mutations in the L gene; however, the specification does not provide any indication that a single amino acid change will result in the desired *ts* phenotype. The prior art implies that a single amino acid change in the RSV L protein of the subgroup A will result in the desired *ts* phenotype (Juhasz et al. Journal of Virology 1997), however, upon close review it is apparent that there are multiple mutations from the wild type virus that actually lead to the desired phenotype (Juhasz et al., see table 1). Specifically, in the prior art the RSV subgroup A mutant (*cpts*530) has 6 mutations when compared to the wild type RSV A2wt virus and it is important to note that these mutations are not limited to the L protein alone. The incompletely attenuated phenotype *cp*RSV also has 6 mutations but is not as temperature sensitive as the *cpts*530 mutant. The relationship between the sequence of a protein and its tertiary structure (i.e. its activity) are not well understood and is not predictable (e.g. see Ngo et al., (V), in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.). Because of this lack of predictability, extended experimentation would be required to determine which substitution or combination of substitution inside and possibly outside of the L protein is required to achieve the attenuated phenotype desired.

Additionally, there are many different viral strains that belong to the RSV subgroup B, it is not clear that the mutations contemplated (specifically in claim 2) would give rise the desired

phenotype (temperature sensitivity) from other wild type viral isolates RSV (Venter et al. Journal of General Virology, 2001). Therefore, the instant invention is not enabled for the full scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by Randolph et al., (U.S. Pat. No. 5,932,222).

The instant invention is drawn to an isolated, attenuated human RSV subgroup B virus which has at least one attenuating mutation in the RNA polymerase gene. For this office action, the preamble reciting "recombinantly-generated" is interpreted as a product by process, therefore, claims 1-4 were interpreted as "an isolated attenuated RSV virus" (which is a *product*). Product-by-process claims are not limited to the manipulations of the recited steps, only to the structure implied by the steps. M.P.E.P. Section 2113 states that:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made

> by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted)

Randolph et al. disclose the mutation, characterization and isolation of various *ts* attenuations of RSV subgroup B virus. These attenuated viruses have been deposited with ATCC under the following accession numbers #VR2364 (=2R33F) and #VR2365 (=2B20L). The reference discloses using these attenuated viruses as a vaccine formulation (see claims 7-10). The mere recitation of the actual nucleotide sequences (see instant specification tables 21-22) that are inherently possessed by the attenuated viruses in the prior art, does not cause the claim drawn to those things to distinguish over the prior art (See *In re Best, Bolton, and Shaw* 195 USPQ 430 (CCPA 1977), *In re Schreiber* 44 USPQ2d 1429). Therefore, the instant invention is anticipated by Randolph et al.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Randolph et al. (EP 0 567 100 A1).

The instant invention is drawn to an isolated, attenuated human RSV subgroup B virus which has at least one attenuating mutation in the RNA polymerase gene. For this office action, the preamble reciting "recombinantly-generated" is interpreted as a product by process, therefore, claims 1-4 were interpreted as "an isolated attenuated RSV virus" (which is a *product*). Product-by-process claims are not limited to the manipulations of the recited steps, only to the structure implied by the steps. M.P.E.P. Section 2113 states that:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made

by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted)

Randolph et al. disclose the mutation, characterization and isolation of various *ts* attenuations of RSV subgroup B virus, these isolates are designated as 2Bp33F (=2R33F) and 2Bp20L (=2B20L). The reference discloses using these attenuated viruses as a vaccine formulation (see claims 5-6, and tables 14, 16, 17, 18). The mere recitation of the actual nucleotide sequences (see instant specification tables 21-22) that are inherently possessed by the attenuated viruses in the prior art, does not cause the claim drawn to those things to distinguish over the prior art (See *In re Best, Bolton, and Shaw* 195 USPQ 430 (CCPA 1977), *In re Schreiber* 44 USPQ2d 1429).. Therefore, the instant invention is anticipated by Randolph et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-10 of U.S. Patent No. 5,932,222. Although the conflicting claims are not identical, they are not patentably distinct from each other because the

preamble reciting "recombinantly-generated" is interpreted as a product-by-process, therefore, claims 1-4 were interpreted as "an isolated attenuated RSV virus" (which is a *product*). Product-by-process claims are not limited to the manipulations of the recited steps, only to the structure implied by the steps (see above). Randolph et al. disclose the mutation, characterization and isolation of various *ts* attenuations of RSV subgroup B virus. These attenuated viruses have been deposited with ATCC under the following accession numbers #VR2364 (=2R33F) and #VR2365 (=2B20L). The reference discloses using these attenuated viruses as a vaccine formulation (see claims 7-10). The mere recitation of the actual nucleotide sequences (see instant specification tables 21-22) that are inherently possessed by the attenuated viruses in the prior art, does not cause the claim drawn to those things to distinguish over the prior patent.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D.

JAMES HOUSEL 12/3/01
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600